Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID:SSSPTA1626GMS

PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * * * * * * Welcome to STN International * * * * * * * * * *

NEWS 1		Web Page URLs for STN Seminar Schedule - N. America
NEWS 2		"Ask CAS" for self-help around the clock
NEWS 3	JUL 20	Powerful new interactive analysis and visualization software, STN AnaVist, now available
NEWS 4	AUG 11	STN AnaVist workshops to be held in North America
NEWS 5	AUG 30	CA/CAplus -Increased access to 19th century research documents
NEWS 6	AUG 30	CASREACT - Enhanced with displayable reaction conditions
NEWS 7	SEP 09	ACD predicted properties enhanced in REGISTRY/ZREGISTRY
NEWS 8	OCT 03	MATHDI removed from STN
NEWS 9	OCT 04	CA/CAplus-Canadian Intellectual Property Office (CIPO) added to core patent offices
NEWS 10	OCT 06	STN AnaVist workshops to be held in North America
NEWS 11	OCT 13	New CAS Information Use Policies Effective October 17, 2005
NEWS 12	OCT 17	STN(R) AnaVist(TM), Version 1.01, allows the export/download of CAplus documents for use in third-party analysis and visualization tools
NEWS 13	OCT 27	Free KWIC format extended in full-text databases
NEWS 14	OCT 27	DIOGENES content streamlined
NEWS 15	OCT 27	EPFULL enhanced with additional content

NEWS EXPRESS	JUNE 13 CURRENT WINDOWS VERSION IS V8.0, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 13 JUNE 2005
NEWS HOURS	STN Operating Hours Plus Help Desk Availability
NEWS INTER	General Internet Information
NEWS LOGIN	Welcome Banner and News Items
NEWS PHONE	Direct Dial and Telecommunication Network Access to STN
NEWS WWW	CAS World Wide Web Site (general information)

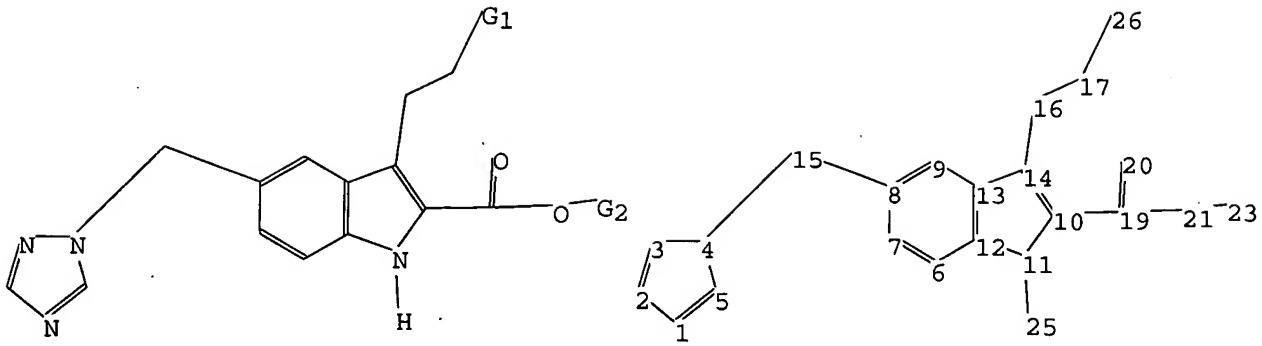
Enter NEWS followed by the item number or name to see news on that specific topic.

All use of STN is subject to the provisions of the STN Customer agreement. Please note that this agreement limits use to scientific research. Use for software development or design or implementation of commercial gateways or other similar uses is prohibited and may result in loss of user privileges and other penalties.

* * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 11:03:33 ON 10 NOV 2005

```
=>
Uploading
THIS COMMAND NOT AVAILABLE IN THE CURRENT FILE
Do you want to switch to the Registry File?
Choice (Y/n):
Switching to the Registry File...
Some commands only work in certain files.  For example, the EXPAND
command can only be used to look at the index in a file which has an
index.  Enter "HELP COMMANDS" at an arrow prompt (=>) for a list of
commands which can be used in this file.

=> FILE REGISTRY

COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     0.21       0.21

FILE 'REGISTRY' ENTERED AT 11:03:47 ON 10 NOV 2005
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2005 American Chemical Society (ACS)

Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES:     8 NOV 2005  HIGHEST RN 866995-49-5
DICTIONARY FILE UPDATES:    8 NOV 2005  HIGHEST RN 866995-49-5

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH JULY 14, 2005

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

*********************************************************************
*                                                                   *
* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added,   *
* effective March 20, 2005.  A new display format, IDERL, is now    *
* available and contains the CA role and document type information. *
*                                                                   *
*********************************************************************

Structure search iteration limits have been increased.  See HELP SLIMITS
for details.

REGISTRY includes numerically searchable data for experimental and
predicted properties as well as tags indicating availability of
experimental property data in the original document.  For information
on property searching in REGISTRY, refer to:

http://www.cas.org/ONLINE/UG/regprops.html

=>
Uploading C:\Program Files\Stnexp\Queries\10509918.str
```



chain nodes :
15 16 17 19 20 21 23 25 26
ring nodes :
1 2 3 4 5 6 7 8 9 10 11 12 13 14
chain bonds :
4-15 8-15 10-19 11-25 14-16 16-17 17-26 19-20 19-21 21-23
ring bonds :
1-2 1-5 2-3 3-4 4-5 6-7 6-12 7-8 8-9 9-13 10-11 10-14 11-12 12-13
13-14
exact/norm bonds :
1-2 1-5 2-3 3-4 4-5 4-15 10-11 11-12 17-26 19-20 19-21 21-23
exact bonds :
8-15 10-14 10-19 11-25 13-14 14-16 16-17
normalized bonds :
6-7 6-12 7-8 8-9 9-13 12-13
isolated ring systems :
containing 1 : 6 :

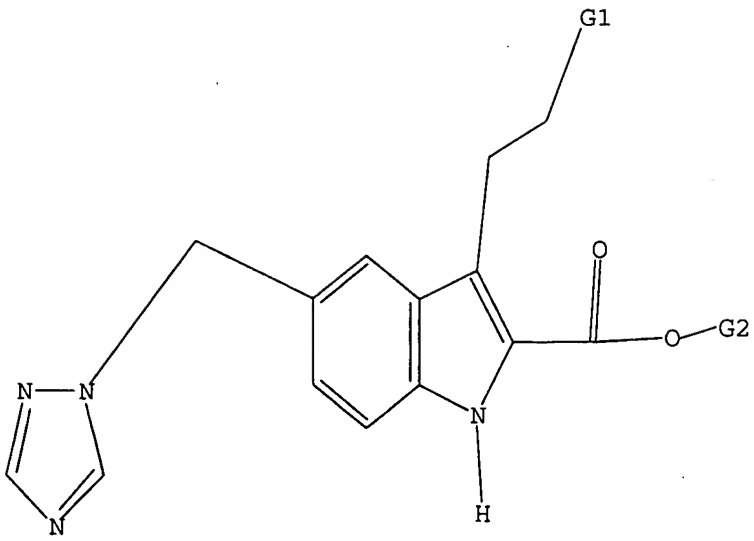
G1:N,CH

G2:H,Ak,CH3,Et

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:Atom 12:Atom 13:Atom 14:Atom 15:CLASS 16:CLASS 17:CLASS 19:CLASS
20:CLASS 21:CLASS 23:CLASS 25:CLASS 26:CLASS

L1 STRUCTURE UPLOADED

=> d l1
L1 HAS NO ANSWERS
L1 STR



G1 N,CH
G2 H,Ak,Me,Et

Structure attributes must be viewed using STN Express query preparation.

```
=> s l1
SAMPLE SEARCH INITIATED 11:04:10 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -        1 TO ITERATE

100.0% PROCESSED         1 ITERATIONS                          0 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:            1 TO        80
PROJECTED ANSWERS:               0 TO         0

L2             0 SEA SSS SAM L1

=> s l1 sss full
FULL SEARCH INITIATED 11:04:16 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -       16 TO ITERATE

100.0% PROCESSED        16 ITERATIONS                          2 ANSWERS
SEARCH TIME: 00.00.01

L3             2 SEA SSS FUL L1

=> FIL HCAPLUS
COST IN U.S. DOLLARS                          SINCE FILE      TOTAL
                                                 ENTRY    SESSION
FULL ESTIMATED COST                             161.33     161.54

FILE 'HCAPLUS' ENTERED AT 11:04:22 ON 10 NOV 2005
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
```

FILE COVERS 1907 - 10 Nov 2005 VOL 143 ISS 20
FILE LAST UPDATED: 9 Nov 2005 (20051109/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

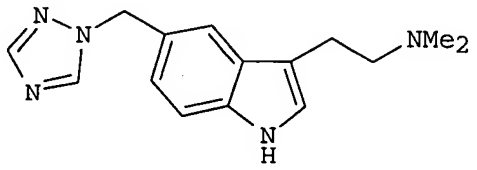
=> s l3
L4 1 L3

=> d l4 ibib abs hitstr tot

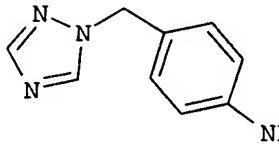
L4 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:143122 HCAPLUS
DOCUMENT NUMBER: 140:181454
TITLE: Process for preparing N,N-Dimethyl-2-[5-(1H-[1,2,4]triazol-1-ylmethyl)-1H-indol-3-yl]ethylamine (rizatriptan) and its salts via Fischer indole reaction, N-alkylation and decarboxylation
INVENTOR(S): Dalmases Barjoan, Pere; Armengol Asparo, Montserrat
PATENT ASSIGNEE(S): Laboratorios Vita, S.A., Spain
SOURCE: PCT Int. Appl., 34 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004014877	A1	20040219	WO 2003-IB3540	20030805
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
ES 2204303	A1	20040416	ES 2002-1874	20020807
ES 2204303	B2	20041216		
EP 1527053	A1	20050504	EP 2003-784405	20030805
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,				

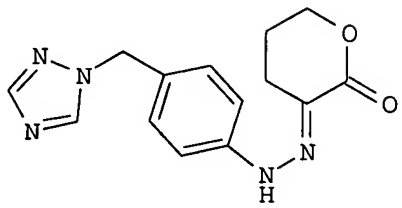
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
US 2005148778 A1 20050707 US 2003-509918 20030805
PRIORITY APPLN. INFO.: ES 2002-1874 A 20020807
WO 2003-IB3540 W 20030805
OTHER SOURCE(S): MARPAT 140:181454
GI



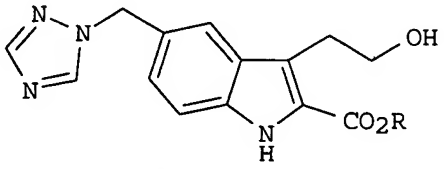
I



II



III



IV

AB The invention is related to a multi-step process for preparing the well-known anti-migraine rizatriptan I or a pharmaceutically acceptable salt by a. diazotization of the aniline (II) hydrochloride; followed by reduction and acidification to ; b. condensation of α-keto-δ-valerolactone with hydrazine hydrochloride to give the hydrazone (III); c. Fischer indole reaction of the hydrazone III, to give a pyranoindolone, optionally followed by a hydrolysis reaction; d. transesterification or esterification of the hydrolysis product, to give IV, [wherein R = straight or branched alkyl]; e. N-alkylation of dimethylamine with IV to give the corresponding alkyl indolecarboxylate f. saponification of the ester; and

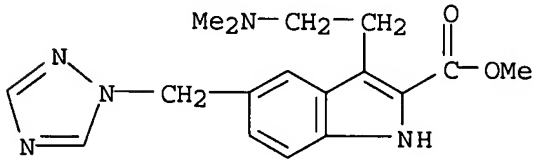
g. decarboxylation of the indolecarboxylic acid to give rizatriptan and, eventually, conversion to a pharmaceutically acceptable salt thereof. The advantages includes easy industrial scale-up by elimination of use of expensive catalysts or highly toxic or highly flammable reagents, and no steps of column purification Thus, I•benzoic acid was obtained via IV (R = Me) by activation of the alc. with tosyl chloride, N-alkylation of dimethylamine in MeOH, KOH-saponification of the ester in EtOH, decarboxylation of the indolecarboxylic acid to free-I in the presence of Cu2O/quinoline, and salt formation by reacting I with benzoic acid in i-PrOH/isopropyl acetate. IV (R = Me) was prepared either by esterification of its acid

(prepared by one-pot synthesis) with methanol in the presence of methanesulfonic acid or by transesterification of pyranoindolone obtained by Fischer indole synthesis of hydrazone III.

IT **658697-15-5P**, 3-(2-Dimethylaminoethyl)-5-[(1H-1,2,4-triazol-1-yl)methyl]-1H-indole-2-carboxylic acid methyl ester
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(indolecarboxylic acid ester intermediate; process for preparing rizatriptan)

RN 658697-15-5 HCAPLUS

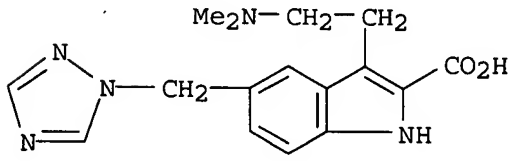
CN 1H-Indole-2-carboxylic acid, 3-[2-(dimethylamino)ethyl]-5-(1H-1,2,4-triazol-1-ylmethyl)-, methyl ester (9CI) (CA INDEX NAME)



IT **658697-16-6P**, 3-(2-Dimethylaminoethyl)-5-[(1H-1,2,4-triazol-1-yl)methyl]-1H-indole-2-carboxylic acid
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(indolecarboxylic acid; process for preparing rizatriptan)

RN 658697-16-6 HCAPLUS

CN 1H-Indole-2-carboxylic acid, 3-[2-(dimethylamino)ethyl]-5-(1H-1,2,4-triazol-1-ylmethyl)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> FIL REGISTRY

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	17.19	178.73

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-0.73	-0.73

FILE 'REGISTRY' ENTERED AT 11:07:08 ON 10 NOV 2005

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 8 NOV 2005 HIGHEST RN 866995-49-5
DICTIONARY FILE UPDATES: 8 NOV 2005 HIGHEST RN 866995-49-5

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH JULY 14, 2005

Please note that search-term pricing does apply when conducting SmartSELECT searches.

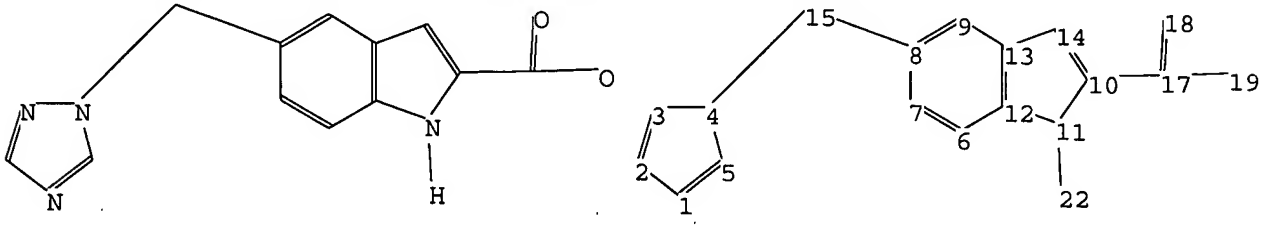
****
* *
* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added, *
* effective March 20, 2005. A new display format, IDERL, is now *
* available and contains the CA role and document type information. *
* *
****

Structure search iteration limits have been increased. See HELP SLIMITS for details.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/ONLINE/UG/regprops.html

=>
Uploading C:\Program Files\Stnexp\Queries\10509918a.str



chain nodes :
15 17 18 19 22
ring nodes :
1 2 3 4 5 6 7 8 9 10 11 12 13 14
chain bonds :
4-15 8-15 10-17 11-22 17-18 17-19
ring bonds :
1-2 1-5 2-3 3-4 4-5 6-7 6-12 7-8 8-9 9-13 10-11 10-14 11-12 12-13 13-14
exact/norm bonds :
1-2 1-5 2-3 3-4 4-5 4-15 10-11 11-12 17-18 17-19
exact bonds :
8-15 10-14 10-17 11-22 13-14
normalized bonds :
6-7 6-12 7-8 8-9 9-13 12-13
isolated ring systems :

containing 1 : 6 :

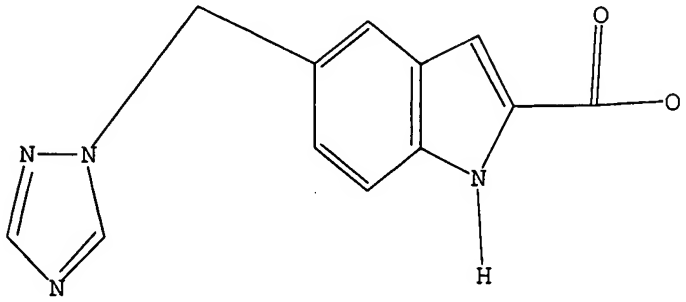
G1:N,CH

G2:H,Ak,CH3,Et

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:Atom 12:Atom 13:Atom 14:Atom 15:CLASS 17:CLASS 18:CLASS 19:CLASS
22:CLASS

L5 STRUCTURE UPLOADED

=> d l5
L5 HAS NO ANSWERS
L5 STR



G1 N,CH
G2 H,Ak,Me,Et

Structure attributes must be viewed using STN Express query preparation.

=> s l5
SAMPLE SEARCH INITIATED 11:07:25 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 18 TO ITERATE

100.0% PROCESSED 18 ITERATIONS 1 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 106 TO 614
PROJECTED ANSWERS: 1 TO 80

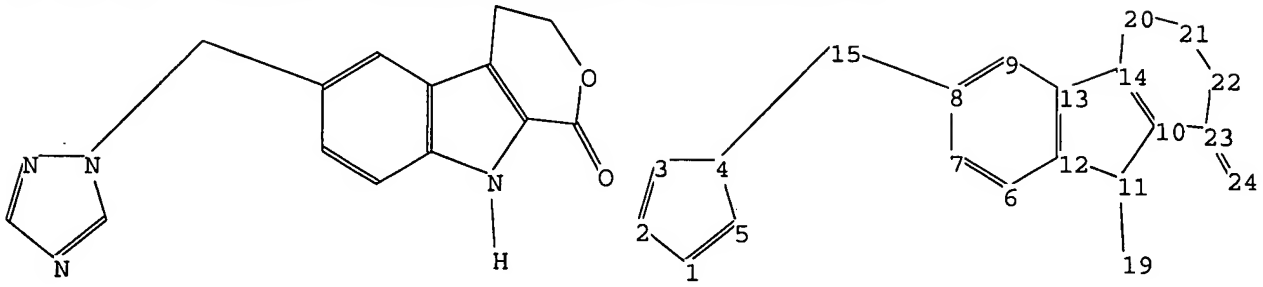
L6 1 SEA SSS SAM L5

=> s l5 sss full
FULL SEARCH INITIATED 11:07:31 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 447 TO ITERATE

100.0% PROCESSED 447 ITERATIONS 5 ANSWERS
SEARCH TIME: 00.00.01

L7 5 SEA SSS FUL L5

=>
Uploading C:\Program Files\Stnexp\Queries\10509918b.str



chain nodes :
15 19 24
ring nodes :
1 2 3 4 5 6 7 8 9 10 11 12 13 14 20 21 22 23
chain bonds :
4-15 8-15 11-19 23-24
ring bonds :
1-2 1-5 2-3 3-4 4-5 6-7 6-12 7-8 8-9 9-13 10-11 10-14 10-23 11-12
12-13 13-14 14-20 20-21 21-22 22-23
exact/norm bonds :
1-2 1-5 2-3 3-4 4-5 4-15 10-11 11-12 23-24
exact bonds :
8-15 10-14 10-23 11-19 13-14 14-20 20-21 21-22 22-23
normalized bonds :
6-7 6-12 7-8 8-9 9-13 12-13
isolated ring systems :
containing 1 : 6 :

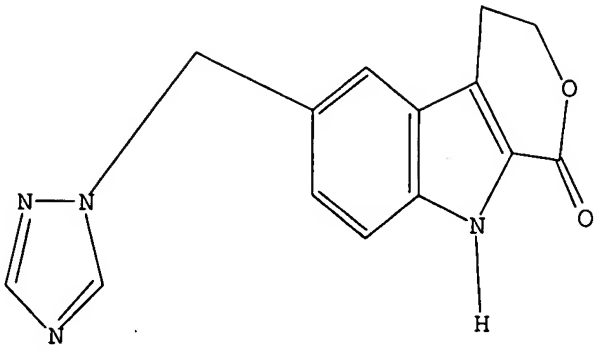
G1:N,CH

G2:H,Ak,CH3,Et

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:Atom 12:Atom 13:Atom 14:Atom 15:CLASS 19:CLASS 20:Atom 21:Atom 22:Atom
23:Atom 24:CLASS

L8 STRUCTURE UPLOADED

=> d 18
L8 HAS NO ANSWERS
L8 STR



G1 N,CH

G2 H,Ak,Me,Et

Structure attributes must be viewed using STN Express query preparation.

```
=> s l8
SAMPLE SEARCH INITIATED 11:10:00 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -        0 TO ITERATE

100.0% PROCESSED         0 ITERATIONS                                0 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:            0 TO         0
PROJECTED ANSWERS:               0 TO         0

L9             0 SEA SSS SAM L8

=> s l8 sss full
FULL SEARCH INITIATED 11:10:06 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -        9 TO ITERATE

100.0% PROCESSED         9 ITERATIONS                                2 ANSWERS
SEARCH TIME: 00.00.01

L10            2 SEA SSS FUL L8

=> FIL HCAPLUS
COST IN U.S. DOLLARS                                  SINCE FILE      TOTAL
                                                         ENTRY    SESSION
FULL ESTIMATED COST                                     323.95     502.68

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)            SINCE FILE      TOTAL
                                                         ENTRY    SESSION
CA SUBSCRIBER PRICE                                       0.00      -0.73

FILE 'HCAPLUS' ENTERED AT 11:10:12 ON 10 NOV 2005
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2005 AMERICAN CHEMICAL SOCIETY (ACS)
```

FILE COVERS 1907 - 10 Nov 2005 VOL 143 ISS 20
FILE LAST UPDATED: 9 Nov 2005 (20051109/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d his

(FILE 'HOME' ENTERED AT 11:03:33 ON 10 NOV 2005)

FILE 'REGISTRY' ENTERED AT 11:03:47 ON 10 NOV 2005
L1 STRUCTURE UPLOADED
L2 0 S L1
L3 2 S L1 SSS FULL

FILE 'HCAPLUS' ENTERED AT 11:04:22 ON 10 NOV 2005
L4 1 S L3

FILE 'REGISTRY' ENTERED AT 11:07:08 ON 10 NOV 2005
L5 STRUCTURE UPLOADED
L6 1 S L5
L7 5 S L5 SSS FULL
L8 STRUCTURE UPLOADED
L9 0 S L8
L10 2 S L8 SSS FULL

FILE 'HCAPLUS' ENTERED AT 11:10:12 ON 10 NOV 2005

=> s l7
L11 1 L7

=> s l10
L12 1 L10

=> d l11 ibib abs hitstr tot

L11 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:143122 HCAPLUS
DOCUMENT NUMBER: 140:181454
TITLE: Process for preparing N,N-Dimethyl-2-[5-(1H-[1,2,4]triazol-1-ylmethyl)-1H-indol-3-yl]ethylamine (rizatriptan) and its salts via Fischer indole reaction, N-alkylation and decarboxylation
INVENTOR(S): Dalmases Barjoan, Pere; Armengol Asparo, Montserrat
PATENT ASSIGNEE(S): Laboratorios Vita, S.A., Spain
SOURCE: PCT Int. Appl., 34 pp.

CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004014877	A1	20040219	WO 2003-IB3540	20030805
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
ES 2204303	A1	20040416	ES 2002-1874	20020807
ES 2204303	B2	20041216		
EP 1527053	A1	20050504	EP 2003-784405	20030805
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
US 2005148778	A1	20050707	US 2003-509918	20030805

PRIORITY APPLN. INFO.: ES 2002-1874 A 20020807
WO 2003-IB3540 W 20030805

OTHER SOURCE(S): MARPAT 140:181454
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

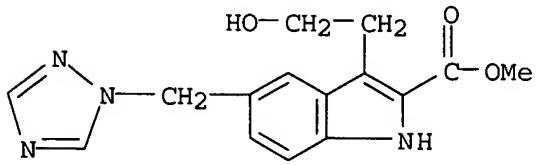
AB The invention is related to a multi-step process for preparing the well-known anti-migraine rizatriptan I or a pharmaceutically acceptable salt by a. diazotization of the aniline (II) hydrochloride; followed by reduction and acidification to ; b. condensation of α-keto-δ-valerolactone with hydrazine hydrochloride to give the hydrazone (III); c. Fischer indole reaction of the hydrazone III, to give a pyranoindolone, optionally followed by a hydrolysis reaction; d. transesterification or esterification of the hydrolysis product, to give IV, [wherein R = straight or branched alkyl]; e. N-alkylation of dimethylamine with IV to give the corresponding alkyl indolecarboxylate f. saponification of the ester; and
g. decarboxylation of the indolecarboxylic acid to give rizatriptan and, eventually, conversion to a pharmaceutically acceptable salt thereof. The advantages includes easy industrial scale-up by elimination of use of expensive catalysts or highly toxic or highly flammable reagents, and no steps of column purification Thus, I•benzoic acid was obtained via IV (R = Me) by activation of the alc. with tosyl chloride, N-alkylation of dimethylamine in MeOH, KOH-saponification of the ester in EtOH, decarboxylation of the indolecarboxylic acid to free-I in the presence of Cu2O/quinoline, and salt formation by reacting I with benzoic acid in i-PrOH/isopropyl acetate. IV (R = Me) was prepared either by esterification of its acid (prepared by one-pot synthesis) with methanol in the presence of methanesulfonic acid or by transesterification of pyranoindolone obtained

by Fischer indole synthesis of hydrazone III.

IT **658697-11-1P**, 3-(2-Hydroxyethyl)-5-[(1H-1,2,4-triazol-1-yl)methyl]-1H-indole-2-carboxylic acid methyl ester
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(hydroxyethylindolyl intermediate; process for preparing rizatriptan)

RN 658697-11-1 HCAPLUS

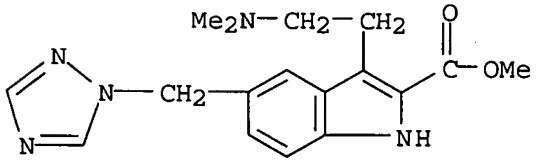
CN 1H-Indole-2-carboxylic acid, 3-(2-hydroxyethyl)-5-(1H-1,2,4-triazol-1-ylmethyl)-, methyl ester (9CI) (CA INDEX NAME)



IT **658697-15-5P**, 3-(2-Dimethylaminoethyl)-5-[(1H-1,2,4-triazol-1-yl)methyl]-1H-indole-2-carboxylic acid methyl ester
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(indolecarboxylic acid ester intermediate; process for preparing rizatriptan)

RN 658697-15-5 HCAPLUS

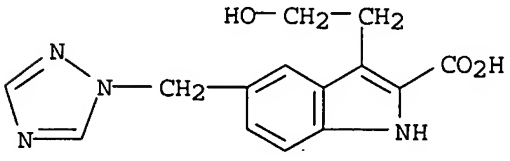
CN 1H-Indole-2-carboxylic acid, 3-[2-(dimethylamino)ethyl]-5-(1H-1,2,4-triazol-1-ylmethyl)-, methyl ester (9CI) (CA INDEX NAME)



IT **658697-10-0P**, 3-(2-Hydroxyethyl)-5-[(1H-1,2,4-triazol-1-yl)methyl]-1H-indole-2-carboxylic acid
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(indolecarboxylic acid intermediate; process for preparing rizatriptan)

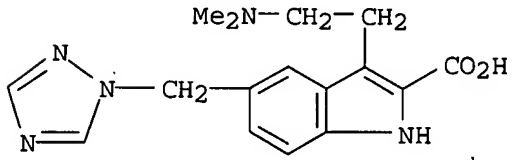
RN 658697-10-0 HCAPLUS

CN 1H-Indole-2-carboxylic acid, 3-(2-hydroxyethyl)-5-(1H-1,2,4-triazol-1-ylmethyl)- (9CI) (CA INDEX NAME)

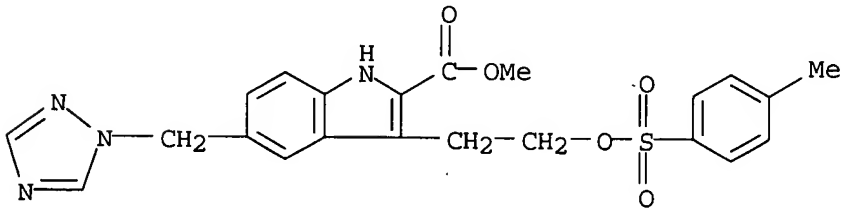


IT **658697-16-6P**, 3-(2-Dimethylaminoethyl)-5-[(1H-1,2,4-triazol-1-yl)methyl]-1H-indole-2-carboxylic acid
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(indolecarboxylic acid; process for preparing rizatriptan)
RN 658697-16-6 HCAPLUS
CN 1H-Indole-2-carboxylic acid, 3-[2-(dimethylamino)ethyl]-5-(1H-1,2,4-triazol-1-ylmethyl)- (9CI) (CA INDEX NAME)



IT **658697-14-4P**, 3-[2-[(4-Tolylsulfonyl)oxy]ethyl]-5-[(1H-1,2,4-triazol-1-yl)methyl]-1H-indole-2-carboxylic acid methyl ester
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(tosylate intermediate; process for preparing rizatriptan)
RN 658697-14-4 HCAPLUS
CN 1H-Indole-2-carboxylic acid, 3-[2-[[(4-methylphenyl)sulfonyl]oxy]ethyl]-5-(1H-1,2,4-triazol-1-ylmethyl)-, methyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d l12 ibib abs hitstr tot

L12 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:143122 HCAPLUS
DOCUMENT NUMBER: 140:181454
TITLE: Process for preparing N,N-Dimethyl-2-[5-(1H-[1,2,4]triazol-1-ylmethyl)-1H-indol-3-yl]ethylamine (rizatriptan) and its salts via Fischer indole reaction, N-alkylation and decarboxylation
INVENTOR(S): Dalmases Barjoan, Pere; Armengol Asparo, Montserrat
PATENT ASSIGNEE(S): Laboratorios Vita, S.A., Spain
SOURCE: PCT Int. Appl., 34 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004014877	A1	20040219	WO 2003-IB3540	20030805

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,

GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM,
PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN,
TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

ES 2204303	A1	20040416	ES 2002-1874	20020807
ES 2204303	B2	20041216		
EP 1527053	A1	20050504	EP 2003-784405	20030805
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
US 2005148778	A1	20050707	US 2003-509918	20030805
PRIORITY APPLN. INFO.:			ES 2002-1874 A	20020807
			WO 2003-IB3540 W	20030805

OTHER SOURCE(S): MARPAT 140:181454
GI

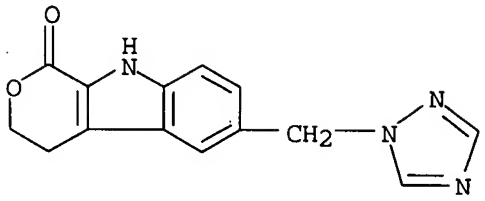
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention is related to a multi-step process for preparing the well-known anti-migraine rizatriptan I or a pharmaceutically acceptable salt by a. diazotization of the aniline (II) hydrochloride; followed by reduction and acidification to ; b. condensation of α-keto-δ-valerolactone with hydrazine hydrochloride to give the hydrazone (III); c. Fischer indole reaction of the hydrazone III, to give a pyranoindolone, optionally followed by a hydrolysis reaction; d. transesterification or esterification of the hydrolysis product, to give IV, [wherein R = straight or branched alkyl]; e. N-alkylation of dimethylamine with IV to give the corresponding alkyl indolecarboxylate f. saponification of the ester; and
g. decarboxylation of the indolecarboxylic acid to give rizatriptan and, eventually, conversion to a pharmaceutically acceptable salt thereof. The advantages includes easy industrial scale-up by elimination of use of expensive catalysts or highly toxic or highly flammable reagents, and no steps of column purification Thus, I•benzoic acid was obtained via IV (R = Me) by activation of the alc. with tosyl chloride, N-alkylation of dimethylamine in MeOH, KOH-saponification of the ester in EtOH, decarboxylation of the indolecarboxylic acid to free-I in the presence of Cu2O/quinoline, and salt formation by reacting I with benzoic acid in i-PrOH/isopropyl acetate. IV (R = Me) was prepared either by esterification of its acid (prepared by one-pot synthesis) with methanol in the presence of methanesulfonic acid or by transesterification of pyranoindolone obtained by Fischer indole synthesis of hydrazone III.

IT **658697-13-3P**, 6-[(1H-1,2,4-Triazol-1-yl)methyl]-4,9-dihydro-3H-pyrano[3,4-b]indol-1-one hydrochloride
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(pyranoindolone intermediate; process for preparing rizatriptan)

RN 658697-13-3 HCAPLUS

CN Pyrano[3,4-b]indol-1(3H)-one, 4,9-dihydro-6-(1H-1,2,4-triazol-1-ylmethyl)-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

```
=> s rizatriptan
L13          267 RIZATRIPTAN

=> s l13 and process
          2167504 PROCESS
          1453092 PROCESSES
          3226621 PROCESS
                    (PROCESS OR PROCESSES)
L14             17 L13 AND PROCESS

=> s l14 and py<=2002
         22790283 PY<=2002
L15             11 L14 AND PY<=2002

=> d his

     (FILE 'HOME' ENTERED AT 11:03:33 ON 10 NOV 2005)

     FILE 'REGISTRY' ENTERED AT 11:03:47 ON 10 NOV 2005
L1                 STRUCTURE UPLOADED
L2               0 S L1
L3               2 S L1 SSS FULL

     FILE 'HCAPLUS' ENTERED AT 11:04:22 ON 10 NOV 2005
L4               1 S L3

     FILE 'REGISTRY' ENTERED AT 11:07:08 ON 10 NOV 2005
L5                 STRUCTURE UPLOADED
L6               1 S L5
L7               5 S L5 SSS FULL
L8                 STRUCTURE UPLOADED
L9               0 S L8
L10              2 S L8 SSS FULL

     FILE 'HCAPLUS' ENTERED AT 11:10:12 ON 10 NOV 2005
L11              1 S L7
L12              1 S L10
L13            267 S RIZATRIPTAN
L14             17 S L13 AND PROCESS
L15             11 S L14 AND PY<=2002

=> d l11 ibib abs hitstr tot
```

L11 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:143122 HCAPLUS
DOCUMENT NUMBER: 140:181454
TITLE: Process for preparing N,N-Dimethyl-2-[5-(1H-[1,2,4]triazol-1-ylmethyl)-1H-indol-3-yl]ethylamine (rizatriptan) and its salts via Fischer indole reaction, N-alkylation and decarboxylation
INVENTOR(S): Dalmases Barjoan, Pere; Armengol Asparo, Montserrat
PATENT ASSIGNEE(S): Laboratorios Vita, S.A., Spain
SOURCE: PCT Int. Appl., 34 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004014877	A1	20040219	WO 2003-IB3540	20030805
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
ES 2204303	A1	20040416	ES 2002-1874	20020807
ES 2204303	B2	20041216		
EP 1527053	A1	20050504	EP 2003-784405	20030805
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
US 2005148778	A1	20050707	US 2003-509918	20030805

PRIORITY APPLN. INFO.: ES 2002-1874 A 20020807
WO 2003-IB3540 W 20030805

OTHER SOURCE(S): MARPAT 140:181454
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

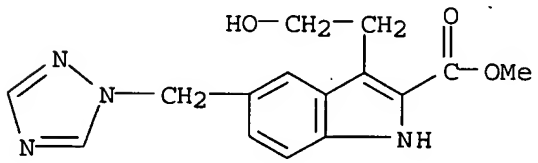
AB The invention is related to a multi-step process for preparing the well-known anti-migraine rizatriptan I or a pharmaceutically acceptable salt by a. diazotization of the aniline (II) hydrochloride; followed by reduction and acidification to ; b. condensation of α-keto-δ-valerolactone with hydrazine hydrochloride to give the hydrazone (III); c. Fischer indole reaction of the hydrazone III, to give a pyranoindolone, optionally followed by a hydrolysis reaction; d. transesterification or esterification of the hydrolysis product, to give IV, [wherein R = straight or branched alkyl]; e. N-alkylation of dimethylamine with IV to give the corresponding alkyl indolecarboxylate f. saponification of the ester; and
g. decarboxylation of the indolecarboxylic acid to give rizatriptan and, eventually, conversion to a pharmaceutically acceptable salt thereof. The

advantages includes easy industrial scale-up by elimination of use of expensive catalysts or highly toxic or highly flammable reagents, and no steps of column purification Thus, I•benzoic acid was obtained via IV (R = Me) by activation of the alc. with tosyl chloride, N-alkylation of dimethylamine in MeOH, KOH-saponification of the ester in EtOH, decarboxylation of the indolecarboxylic acid to free-I in the presence of Cu2O/quinoline, and salt formation by reacting I with benzoic acid in i-PrOH/isopropyl acetate. IV (R = Me) was prepared either by esterification of its acid (prepared by one-pot synthesis) with methanol in the presence of methanesulfonic acid or by transesterification of pyranoindolone obtained by Fischer indole synthesis of hydrazone III.

IT **658697-11-1P**, 3-(2-Hydroxyethyl)-5-[(1H-1,2,4-triazol-1-yl)methyl]-1H-indole-2-carboxylic acid methyl ester
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(hydroxyethylindolyl intermediate; process for preparing rizatriptan)

RN 658697-11-1 HCAPLUS

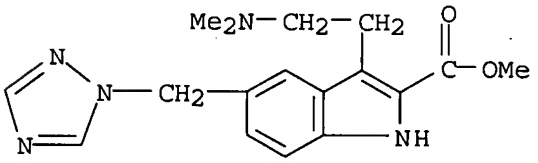
CN 1H-Indole-2-carboxylic acid, 3-(2-hydroxyethyl)-5-(1H-1,2,4-triazol-1-ylmethyl)-, methyl ester (9CI) (CA INDEX NAME)



IT **658697-15-5P**, 3-(2-Dimethylaminoethyl)-5-[(1H-1,2,4-triazol-1-yl)methyl]-1H-indole-2-carboxylic acid methyl ester
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(indolecarboxylic acid ester intermediate; process for preparing rizatriptan)

RN 658697-15-5 HCAPLUS

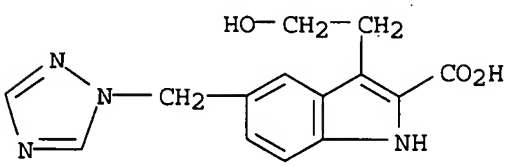
CN 1H-Indole-2-carboxylic acid, 3-[2-(dimethylamino)ethyl]-5-(1H-1,2,4-triazol-1-ylmethyl)-, methyl ester (9CI) (CA INDEX NAME)



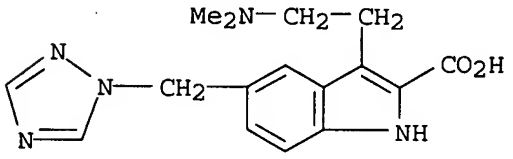
IT **658697-10-0P**, 3-(2-Hydroxyethyl)-5-[(1H-1,2,4-triazol-1-yl)methyl]-1H-indole-2-carboxylic acid
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(indolecarboxylic acid intermediate; process for preparing rizatriptan)

RN 658697-10-0 HCAPLUS

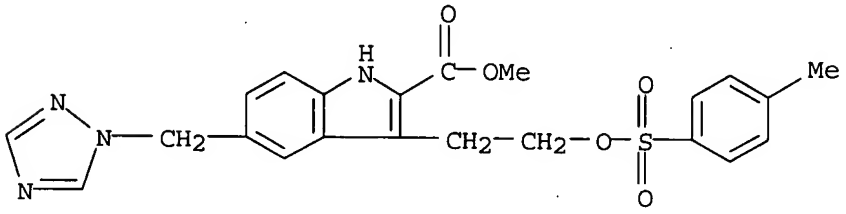
CN 1H-Indole-2-carboxylic acid, 3-(2-hydroxyethyl)-5-(1H-1,2,4-triazol-1-ylmethyl)- (9CI) (CA INDEX NAME)



IT **658697-16-6P**, 3-(2-Dimethylaminoethyl)-5-[(1H-1,2,4-triazol-1-yl)methyl]-1H-indole-2-carboxylic acid
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(indolecarboxylic acid; process for preparing rizatriptan)
RN 658697-16-6 HCAPLUS
CN 1H-Indole-2-carboxylic acid, 3-[2-(dimethylamino)ethyl]-5-(1H-1,2,4-triazol-1-ylmethyl)- (9CI) (CA INDEX NAME)



IT **658697-14-4P**, 3-[2-[(4-Tolylsulfonyl)oxy]ethyl]-5-[(1H-1,2,4-triazol-1-yl)methyl]-1H-indole-2-carboxylic acid methyl ester
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(tosylate intermediate; process for preparing rizatriptan)
RN 658697-14-4 HCAPLUS
CN 1H-Indole-2-carboxylic acid, 3-[2-[[(4-methylphenyl)sulfonyl]oxy]ethyl]-5-(1H-1,2,4-triazol-1-ylmethyl)-, methyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d l12 ibib abs hitstr tot

L12 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:143122 HCAPLUS
DOCUMENT NUMBER: 140:181454
TITLE: Process for preparing N,N-Dimethyl-2-[5-(1H-[1,2,4]triazol-1-ylmethyl)-1H-indol-3-yl]ethylamine (rizatriptan) and its salts via Fischer indole reaction, N-alkylation and decarboxylation
INVENTOR(S): Dalmases Barjoan, Pere; Armengol Asparo, Montserrat
PATENT ASSIGNEE(S): Laboratorios Vita, S.A., Spain
SOURCE: PCT Int. Appl., 34 pp.

CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004014877	A1	20040219	WO 2003-IB3540	20030805
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
ES 2204303	A1	20040416	ES 2002-1874	20020807
ES 2204303	B2	20041216		
EP 1527053	A1	20050504	EP 2003-784405	20030805
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
US 2005148778	A1	20050707	US 2003-509918	20030805

PRIORITY APPLN. INFO.: ES 2002-1874 A 20020807
WO 2003-IB3540 W 20030805

OTHER SOURCE(S): MARPAT 140:181454
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

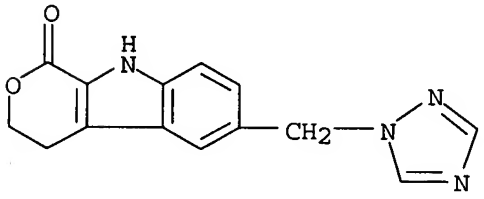
AB The invention is related to a multi-step process for preparing the well-known anti-migraine rizatriptan I or a pharmaceutically acceptable salt by a. diazotization of the aniline (II) hydrochloride; followed by reduction and acidification to ; b. condensation of α-keto-δ-valerolactone with hydrazine hydrochloride to give the hydrazone (III); c. Fischer indole reaction of the hydrazone III, to give a pyranoindolone, optionally followed by a hydrolysis reaction; d. transesterification or esterification of the hydrolysis product, to give IV, [wherein R = straight or branched alkyl]; e. N-alkylation of dimethylamine with IV to give the corresponding alkyl indolecarboxylate f. saponification of the ester; and
g. decarboxylation of the indolecarboxylic acid to give rizatriptan and, eventually, conversion to a pharmaceutically acceptable salt thereof. The advantages includes easy industrial scale-up by elimination of use of expensive catalysts or highly toxic or highly flammable reagents, and no steps of column purification Thus, I•benzoic acid was obtained via IV (R = Me) by activation of the alc. with tosyl chloride, N-alkylation of dimethylamine in MeOH, KOH-saponification of the ester in EtOH, decarboxylation of the indolecarboxylic acid to free-I in the presence of Cu2O/quinoline, and salt formation by reacting I with benzoic acid in i-PrOH/isopropyl acetate. IV (R = Me) was prepared either by esterification of its acid (prepared by one-pot synthesis) with methanol in the presence of methanesulfonic acid or by transesterification of pyranoindolone obtained

by Fischer indole synthesis of hydrazone III.

IT **658697-13-3P**, 6-[(1H-1,2,4-Triazol-1-yl)methyl]-4,9-dihydro-3H-pyrano[3,4-b]indol-1-one hydrochloride
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(pyranoindolone intermediate; process for preparing rizatriptan)

RN 658697-13-3 HCAPLUS

CN Pyrano[3,4-b]indol-1(3H)-one, 4,9-dihydro-6-(1H-1,2,4-triazol-1-ylmethyl)-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d l15 ibib abs hitstr tot

L15 ANSWER 1 OF 11 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:100806 HCAPLUS
DOCUMENT NUMBER: 140:151960
TITLE: Fast-dispersing dosage form containing 5-HT1 agonists
INVENTOR(S): Green, Richard David; Lacy, Jonathan; Mallard, Nicholas; Johnson, Edward
PATENT ASSIGNEE(S): UK
SOURCE: U.S. Pat. Appl. Publ., 12 pp., Cont.-in-part of U.S. Ser. No. 408,595, abandoned.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004023948	A1	20040205	US 2003-375560	20030226
WO 9842344	A1	19981001	WO 1998-GB885	19980324 <--

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: GB 1997-6089 A 19970324
WO 1998-GB885 A1 19980324

US 1999-408595 B2 19990923

AB This invention relates to a pharmaceutical composition for oral administration comprising a carrier and, as an active ingredient, a 5-HT1 agonist, characterized in that the composition is formulated to reduce pre-systemic metabolism of the 5-HT1 agonist. A **process** for preparing such a composition and the use of such a composition for the treatment of anxiety, depression, attention deficit disorder and/or panic disorders and/or as a memory enhancer are also provided. Thus, a fast-dispersing dosage form contained water 89.550, buspirone-HCl 1.200, gelatin 4.000, mannitol 3.000, glycine 1.000, banana flavor 0.250, raspberry flavor 0.250, and aspartame 0.750% by weight

L15 ANSWER 2 OF 11 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:777120 HCAPLUS
DOCUMENT NUMBER: 139:265812
TITLE: **Process** for the preparation of rapidly disintegrating tablet
INVENTOR(S): Lee, Chang-Hyun; Woo, Jong-Soo; Chang, Hee-Chul
PATENT ASSIGNEE(S): Hanmi Pharm. Co., Ltd., S. Korea
SOURCE: U.S. Pat. Appl. Publ., 8 pp., Cont.-in-part of U.S. Pat. Appl. 2002 1,617.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003185886	A1	20031002	US 2003-391103	20030317
US 2002001617	A1	20020103	US 2001-865264	20010525 <--
PRIORITY APPLN. INFO.:			KR 2000-28667 A	20000526
			US 2001-865264 A2	20010525

AB The present invention relates to a **process** for the preparation of a tablet having an enhanced strength as well as a high disintegrating rate in the oral cavity, which comprises: spray-drying an active ingredient to obtain a spray-dried particulate containing the active ingredient; mixing the spray-dried particulate, a sublimable substance suitable for oral administration, a poly(ethylene glycol), and a pharmaceutically acceptable additive; tableting the mixture; and drying the resulting tablet to sublime the sublimable substance until the tablet becomes porous. For example, ondansetron was dissolved in methanol and the solution was subjected to spray drying to obtain a particulate material, then the particulate was mixed with menthol, mannitol, xylitol, polyethylene glycol, stevioside, PVP, Mg stearate, and silica. The resulting mixture was tableted and dried at 45° for 24 h to sublime menthol to obtain a rapidly disintegrating tablet.

L15 ANSWER 3 OF 11 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:319266 HCAPLUS
DOCUMENT NUMBER: 138:343857
TITLE: Pharmaceutical formulations and systems for improved absorption and multistage release of active agents
INVENTOR(S): Chen, Feng-Jing; Venkateshwaran, Srinivasan; Krill, Steven L.; Patel, Mahesh V.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 55 pp., Cont.-in-part of U.S. Ser. No. 898,553.
CODEN: USXXCO

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 12
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003077297	A1	20030424	US 2002-74687	20020211
US 6294192	B1	20010925	US 1999-258654	19990226 <--
US 6267985	B1	20010731	US 1999-345615	19990630 <--
US 6248363	B1	20010619	US 1999-447690	19991123 <--
US 2003064097	A1	20030403	US 2001-800593	20010306
US 6569463	B2	20030527		
US 2002032171	A1	20020314	US 2001-877541	20010608 <--
US 6761903	B2	20040713		
US 2002012680	A1	20020131	US 2001-898553	20010702 <--
US 6451339	B2	20020917		
WO 2003068186	A1	20030821	WO 2003-US4195	20030211

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:

US 1999-258654	A1	19990226
US 1999-345615	A2	19990630
US 1999-447690	A3	19991123
US 2001-800593	A2	20010306
US 2001-877541	A2	20010608
US 2001-898553	A2	20010702
US 1999-375636	A2	19990817
US 2000-751968	A2	20001229
US 2002-74687	A	20020211

AB The present invention pertains to pharmaceutical formulations and systems for delivery of active agents, wherein a first fraction of an active agent is suspended in a vehicle and a second fraction of active agent is solubilized in the vehicle, with the suspended fraction representing about 5 weight % to about 80 weight % of the active agent and the second fraction representing about 20 weight % to about 95 weight % of the active agent. One or more addnl. active agents, which may be fully solubilized, partially solubilized, or suspended, may also be present. The first and second fractions of the active agent may or may not have different release profiles. Generally, a significant fraction of the solubilized drug will release rapidly, providing for rapid onset, while the suspended drug may be formulated for delayed and/or sustained release. A pharmaceutical suspension contained isotretinoin 40, soybean oil 200, Maisine 35-1 100, and Lutrol F68 100 mg.

L15 ANSWER 4 OF 11 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:777891 HCAPLUS
DOCUMENT NUMBER: 137:309600
TITLE: Chemoenzymic method for producing tryptamine derivatives
INVENTOR(S): Kilgore, James L.; Rozzell, J. David, Jr.

PATENT ASSIGNEE(S): Biocatalytics, Inc., USA
SOURCE: PCT Int. Appl., 36 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002079153	A1	20021010	WO 2002-US9929	20020328 <--
W: JP				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR				
US 2003096379	A1	20030522	US 2002-112253	20020328
PRIORITY APPLN. INFO.:			US 2001-279876P	P 20010328

OTHER SOURCE(S): MARPAT 137:309600

AB The invention relates to a coupled enzymic **process** for producing tryptamine derivs. from indole compds. In the first enzyme-catalyzed reaction, indole derivs. are converted to tryptophan derivative intermediates, then the tryptophan intermediates are decarboxylated in a second enzymic reaction in the same reaction system. In this way, tryptamine derivative products are formed from indole derivs. in a single **process.** The invention is also directed to novel tryptophan and tryptamine derivs., which can be prepared by the inventive method.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 5 OF 11 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:106860 HCAPLUS
DOCUMENT NUMBER: 136:304182
TITLE: Molecular cloning and expression of the porcine trigeminal ganglion cDNA encoding a 5-ht1F receptor
AUTHOR(S): Bhalla, Pankaj; Sharma, Hari S.; Wurch, Thierry; Pauwels, Petrus J.; Saxena, Pramod R.
CORPORATE SOURCE: Department of Pharmacology, Erasmus University Medical Centre Rotterdam, Rotterdam, 3000 DR, Neth.
SOURCE: European Journal of Pharmacology (**2002**), 436(1-2), 23-33
CODEN: EJPHAZ; ISSN: 0014-2999
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Using a combination of reverse transcription polymerase chain reaction (RT-PCR) and inverse-PCR techniques, the authors amplified, cloned and sequenced a full-length porcine 5-hydroxytryptamine 1F (5-ht1F) receptor cDNA derived from porcine trigeminal ganglion. Sequence anal. revealed 1101 base pairs (bp) encoding an open reading frame of 366 amino acids showing a high similarity (>90%) with the 5-ht1F receptor sequences from other species, including human. The recombinant porcine 5-ht1F receptor was expressed in African green monkey kidney cell lines (COS-7 cells) and its ligand binding profile was determined using [3H]5-HT. The affinities of several agonists (LY334370 (5-(4-fluorobenzoyl)amino-3-(1-methylpiperidin-4-yl)-1H-indole fumarate) > CP122638 (N-methyl-3 [pyrrolidin 2(R)-yl methyl]-1H-indol-5-ylmethyl sulfonamide) = naratriptan = 5-HT > eletriptan > sumatriptan > frovatriptan = avitriptan > dihydroergotamine > zolmitriptan > 5-carboxamidotryptamine > **rizatriptan** > alniditan = donitriptan > L694247 (2-[5-[3-(4-methylsulfonylamino)benzyl-1,2,4-oxadiazol-5-yl]-1H-indole-3-yl] ethylamine)) and putative antagonists

(methiothepin > GR127935 (N-[4-methoxy-3-(4-methyl-1-piperazinyl) phenyl]-2'-Me 4'-(5-methyl-1,2,4-oxadiazol-3-yl) [1,1-biphenyl]-4-carboxamide hydrochloride) > ritanserin > SB224289 (2,3,6,7-tetrahydro-1'-methyl-5-[2'-methyl-4'(5-methyl-1,2,4-oxadiazol-3-yl) biphenyl-4-carbonyl] furo [2,3-f] indole-3-spiro-4'-piperidine hydrochloride) > BRL15572 ([1-(3-chlorophenyl)-4-[3,3-diphenyl (2-(S,R)) hydroxypropanylpiperazine] hydrochloride]) > ketanserin = pindolol) correlated highly with those described for the recombinant human 5-ht1F receptor (Spearman correlation coefficient; rs= 0.942). Nevertheless, as compared to the human homolog, some triptans (i.e., sumatriptan, zolmitriptan and **rizatriptan**) displayed a 10- to 15-fold lower affinity for the porcine 5-ht1F receptor. Using RT-PCR technique, the expression of porcine 5-ht1F receptor mRNA was observed in cerebral cortex, trigeminal ganglion and several blood vessels, but not in skeletal muscles. In conclusion, the authors have cloned and established the amino acid sequence and ligand binding profile of the porcine 5-ht1F receptor as well as the distribution of its mRNA. This information may be helpful in exploring the role of 5-ht1F receptor in physiol. **processes** and diseases, such as migraine.

REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 6 OF 11 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2000:841515 HCAPLUS

DOCUMENT NUMBER: 134:250277

TITLE: The role of serotonin and other neuroactive molecules in the physiopathogenesis of migraine: current hypotheses

AUTHOR(S): Hamon, M.; Bourgoin, S.

CORPORATE SOURCE: Inserm U288, faculte de medecine Pitie-Salpetriere, Paris, 75634, Fr.

SOURCE: Pathologie Biologie (**2000**), 48(7), 619-629
CODEN: PTBIAN; ISSN: 0031-3009

PUBLISHER: Editions Scientifiques et Medicales Elsevier

DOCUMENT TYPE: Journal; General Review

LANGUAGE: French

AB A review, with 66 refs. The study of the mechanisms of action of the triptan group of drugs has largely contributed to the progress made in the understanding of the physiopathol. **processes** that are possibly responsible for migraine. In this context, two discoveries have been especially important: 1) these anti-migraine drugs are specifically recognized by three main types of serotonin receptors (5-HT1B, 5-HT1D, and 5-HT1F); and 2) these receptors are present in the meninges, where they are expressed by both smooth muscle cells and/or endothelial cells of the vascular wall and/or the perivascular trigeminal to be deleted axon terminals. These two findings have led to the most currently accepted physiopathogenic hypothesis, whereby the migraine attack would start with an excitation of the perivascular trigeminal to be deleted fibers, which would then trigger the release of vasoactive peptides (substance P, calcitonin gene-related peptide/CGRP) within the dura mater. Locally, i.e., in the dura mater in particular, these substances can provoke vasodilatation (CGRP) and plasmatic extravasation (substance P) with platelet lysis and mast cell degranulation, thereby leading to the release of algogenic substances that excite the neighboring trigeminal fibers, and this neurogenic inflammatory response can progressively extend to the meninges as a whole. This reaction subsequently reaches the bulbar and thalamic nuclei and then the sensory cortex, where it is integrated and expressed as migraine pain. The aim of this article was to report the main findings on endogenous substances (serotonin, peptides, nitric oxide [NO], etc.) which appear to

play a key role in this physiopathogenic sequence.
REFERENCE COUNT: 66 THERE ARE 66 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 7 OF 11 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:821044 HCAPLUS
DOCUMENT NUMBER: 135:28987
TITLE: Vascular effects of 5-HT1B/1D-receptor agonists in patients with migraine headaches
AUTHOR(S): de Hoon, Jan N. J. M.; Willigers, Jean M.; Troost, Jaap; Struijker-Boudier, Harry A. J.; Van Bortel, Luc M. A. B.
CORPORATE SOURCE: Department of Pharmacology and Toxicology, Cardiovascular Research Institute, Maastricht, 6200 MD, Neth.
SOURCE: Clinical Pharmacology & Therapeutics (St. Louis) (**2000**), 68(4), 418-426
CODEN: CLPTAT; ISSN: 0009-9236
PUBLISHER: Mosby, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Second-generation triptans are believed to have fewer cardiovascular effects than sumatriptan. This was investigated in vivo by comparing the vascular effects of equipotent therapeutic dosages of selective 5-HT1B/1D-receptor agonists. Sixteen patients with migraine headaches completed a double-blind, placebo-controlled, four-way crossover study. With ultrasonog. and applanation tonometry used 1.5 h after the oral intake of sumatriptan (50 mg), **rizatriptan** (10 mg), zolmitriptan (2.5 mg), or placebo arterial vessel wall properties, blood flow and pressure waveforms were measured in common carotid, brachial, and temporal arteries. At the brachial artery, flow-induced vasodilation (an endothelium-dependent **process**) was evaluated, and blood pressures were recorded. Mean arterial pressure, 91±2 mm Hg after placebo, increased ($P < .05$) by 4% to 6% after administration of each triptan. Each active treatment decreased ($P < .001$) both brachial and carotid artery diameter Isobaric compliance of the brachial artery, 0.077±0.010 mm2/kPa after placebo, decreased ($P < .01$) by 11% ± 8%, 11% ± 11%, and 23% ± 7% after administration of sumatriptan, **rizatriptan**, and zolmitriptan, resp. Isobaric compliance of the carotid artery was 1.31±0.10 mm2/kPa after placebo (no change). Zolmitriptan was the only triptan that decreased temporal artery diameter significantly (by 12% ± 3%, $P < .001$). The resistance of the temporal artery vascular bed increased after administration of sumatriptan (by 26% ± 11%, $P < .05$) and zolmitriptan (by 40% ± 9%, $P = .001$). Flow-induced vasodilation was unaffected. Selective 5-HT1B/1D-receptor agonists induce vasoconstriction and decrease compliance of conduit arteries. These effects are more pronounced at muscular (temporal, brachial) compared with elastic (carotid) arteries. Resistance is only increased at the temporal artery vascular bed, suggesting cranioselectivity for resistance vessels. Endothelial function is not differently affected by any of the triptans tested.
REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 8 OF 11 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:375684 HCAPLUS
DOCUMENT NUMBER: 133:159633
TITLE: QSAR Model for Drug Human Oral Bioavailability
AUTHOR(S): Yoshida, Fumitaka; Topliss, John G.

CORPORATE SOURCE: Division of Medicinal Chemistry College of Pharmacy, University of Michigan, Ann Arbor, MI, 48109-1065, USA
SOURCE: Journal of Medicinal Chemistry (**2000**), 43(13), 2575-2585
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The quant. structure-bioavailability relationship of 232 structurally diverse drugs was studied to evaluate the feasibility of constructing a predictive model for the human oral bioavailability of prospective new medicinal agents. The oral bioavailability determined in human adults was assigned one of four ratings and analyzed in relation to physicochem. and structural factors by the ORMUCS (ordered multicategorical classification method using the simplex technique) method. A systematic examination of various physicochem. parameters relating primarily to absorption, and structural elements which could influence metabolism, was carried out to analyze their effects on the bioavailability classification of drugs in the data set. Lipophilicity, expressed as the distribution coefficient at pH 6.5, was found to be a significant factor influencing bioavailability. The observation that acids generally had better bioavailability characteristics than bases, with neutral compds. between, led to the formulation of a new parameter, Δ log D (log D6.5 - log D7.4), which proved to be an important contributor in improving the classification results. The addition of 15 structural descriptors relating primarily to well-known metabolic **processes** yielded a satisfactory QSAR equation which had a correct classification rate of 71% (97% within one class) and a Spearman rank correlation coefficient (Rs) of 0.851, despite the diversity of structure and pharmacol. activity in the compound set. In leave-one-out tests, an average of 67% of drugs were correctly classified (96% within one class) with an Rs of 0.812. The relationship formulated identified significant factors influencing bioavailability and assigned them quant. values expressing their contribution. The predictive power of the model was evaluated using a sep. test set of 40 compds., of which 60% (95% within one class) were correctly classified. Since the necessary physicochem. parameters can be calculated or estimated and the structural descriptors are obtained from an inspection of the structure, the model enables a rough estimate to be made of the prospective human oral bioavailability of unsynthesized compds. Also, the model has the advantage of transparency in that it indicates which factors may affect bioavailability and the extent of that effect. This could be useful in designing compds. which are more bioavailable. Refinement of the model is possible as more bioavailability data becomes available. Potential uses are in drug design, prioritization of compds. for synthesis, and selection for detailed studies of early compound leads in drug discovery programs.

REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 9 OF 11 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1998:749148 HCAPLUS
DOCUMENT NUMBER: 130:162588
TITLE: Serotonin 5-HT1B/1D receptor agonists in migraine: comparative pharmacology and its therapeutic implications
AUTHOR(S): Goadsby, Peter J.
CORPORATE SOURCE: Institute of Neurology, National Hospital for Neurology and Neurosurgery, London, UK
SOURCE: CNS Drugs (**1998**), 10(4), 271-286
CODEN: CNDREF; ISSN: 1172-7047

PUBLISHER: Adis International Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with 135 refs. The development and clin. use of the serotonin 5-HT1 receptor agonists, collectively known as the "triptans", has ushered in a new age for clinicians treating patients with migraine, as well as a new era for those who respond to the medicines. The triptans that are currently in use (sumatriptan, naratriptan, **rizatriptan** and zolmitriptan) and those in development [almotriptan, eletriptan and frovatriptan (SB-209509, VML-251)] all share a common pharmacol. of 5-HT1B/1D receptor agonist activity. Administration of a triptan during an acute migraine is aimed, via an interruption of the pathophysiol. of this disorder, at rapid and well tolerated relief of headache and associated symptoms of migraine. Migraine probably involves a combination of cranial vasodilatation, with peripheral trigeminal nerve activation and consequent excitation of trigeminal neurons within the caudal brainstem and upper cervical spinal cord (the trigeminocervical complex). Triptans may act by constricting cranial vessels through 5-HT1B receptors, by inhibiting peripheral trigeminal nerve afferents that innervate the vessels and pain-producing dura mater through 5-HT1D receptors, or by inhibiting central trigeminal neuronal traffic through 5-HT1D receptors, or by a combination of these mechanisms. Peripheral neuronal inhibition is likely to involve inhibition of calcitonin gene-related peptide (CGRP) release and perhaps to some degree inhibition of a trigeminally driven inflammatory **process.** Some aspects of the pharmacokinetics of the various triptans, such as the relationship between time to reach peak plasma concns. and half-lives and clin. efficacy, may reveal information about the fundamental **processes** at work in acute migraine. The triptans have been a source of considerable interest because they have provided important clues to the basic pathophysiol. of migraine and point to an important role for the CNS in this disorder.
REFERENCE COUNT: 135 THERE ARE 135 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 10 OF 11 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1998:672467 HCAPLUS
DOCUMENT NUMBER: 129:321172
TITLE: Pharmaceutical compositions containing 5-HT1 agonists
INVENTOR(S): Green, Richard David; Johnson, Edward Stewart; Lacy, Jonathan Ernest; Mallard, Nicholas John
PATENT ASSIGNEE(S): R. P. Scherer Limited, UK
SOURCE: PCT Int. Appl., 44 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9842344	A1	19981001	WO 1998-GB885	19980324 <--

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM,

GA, GN, ML, MR, NE, SN, TD, TG

AU 9867402	A1	19981020	AU 1998-67402	19980324 <--
EP 969842	A1	20000112	EP 1998-912622	19980324 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2001518925	T2	20011016	JP 1998-545235	19980324 <--
US 2004023948	A1	20040205	US 2003-375560	20030226
PRIORITY APPLN. INFO.:			GB 1997-6089 A	19970324
			WO 1998-GB885 W	19980324
			US 1999-408595 B2	19990923

AB This invention relates to a pharmaceutical composition for oral administration comprising a carrier and, as an active ingredient, a 5-HT1 agonist, characterized in that the composition is formulated to reduce pre-systemic metabolism of the 5-HT1 agonist. A **process** for preparing such a composition and the use of such a composition for the treatment of anxiety, depression, attention deficit disorder and/or panic disorders and/or as a memory enhancer are also provided. Fast dispersing dosage forms were prepared from water 223.875, buspirone-HCl 3.000, gelatin EP 10.000, mannitol 7.500, glycine 2.500, banana flavor 0.625, raspberry flavor 0.625, and aspartame 1.875 mg.

REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 11 OF 11 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:	1998:414053 HCAPLUS
DOCUMENT NUMBER:	129:72312
TITLE:	The reversed-phase liquid chromatographic behavior of the new 5-HT1D receptor agonist **rizatriptan** benzoate and its potential **process** impurities
AUTHOR(S):	Antonucci, Vincent; Wright, Lisa; Toma, Pascal
CORPORATE SOURCE:	Merck Research Laboratories, Analytical Research Department Merck and Co., Inc., Rahway, NJ, 07065-0914, USA
SOURCE:	Journal of Liquid Chromatography & Related Technologies (**1998**), 21(11), 1649-1670 CODEN: JLCTFC; ISSN: 1082-6076
PUBLISHER:	Marcel Dekker, Inc.
DOCUMENT TYPE:	Journal
LANGUAGE:	English

AB The reversed-phase chromatog. behavior of the powerful new anti-migraine drug **rizatriptan** benzoate and its potential impurities has been studied. Mol. dynamics calcns. were used to explain the elution order of the two regioisomers of **rizatriptan** formed during its synthesis in terms of conformational differences. Further, van't Hoff plots for a mixture of the two regioisomers and one potential **process** impurity were non-linear (R = 0.937 - 0.965) when chromatographed on an SB-Ph column. However, van't Hoff plots for the same analytes were linear (R ≥ 0.996) when chromatographed on an C8 column. The break in the van't Hoff plots generated with an SB-Ph phase occurs at ambient temperature (.apprx.25°C) and is attributed to changes in stationary phase morphol. as a function of temperature The SB-Ph phase is believed to orient itself in a much more rigid state at sub-ambient temps. than at temps. above ambient, which results in the observed reduction in the enthalpy of interaction for analytes at sub-ambient temperature A corresponding decrease in separation factor (ln α) between **rizatriptan** regioisomers with increasing temperature is observed as the shape selectivity of the SB-Ph stationary

phase decreases.
REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> log y

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	63.61	566.29

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-10.95	-11.68

STN INTERNATIONAL LOGOFF AT 11:13:36 ON 10 NOV 2005